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Commentary

Forecasting Nutrition Research in 2020

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Advances in nutrition during the past century have helped untold numbers of people around the world enjoy healthier and longer lives and be more productive members of society. These advances include the identification of numerous essential nutrients, the identification of common disease states that can arise as a consequence of deficiencies of these essential nutrients, the use of food fortification to correct common deficiencies in the diet, and improvements in agricultural practices and food processing that have resulted in marked advances in food safety and quality. However, many challenges still remain. To a significant extent, these challenges reflect expectations of what constitutes a good diet and what the result of following food guidelines will produce. Moving forward in time in an era of limited economic resources and expanding populations, a critical focus is required to direct attention to the most pressing challenges with the greatest need and opportunity for return on investment. Balancing the desire for quick and effective solutions with the slow, steady, and incremental nature of nutrition research is a struggle confronting academia, industry, and government.

To address these challenges, a group of distinguished nutrition scientists gathered for a panel symposium in celebration of the 10th anniversary of the Kosuna Distinguished Lecture in Nutrition at the University of California, Davis. Eight of the panelists were previous Kosuna Distinguished Lecturers. The symposium discussion revolved around 2 questions that were posed to the panel members prior to the meeting: (1) What will be the "hottest" areas of nutrition research in 2020 and (2) If one were just starting a career in nutrition, what would be a reasonable focus for one's work? A distillation of the discussion follows, organized from the most global to the most individual topics, with some concluding thoughts on the nature of nutrition research.

WHAT WILL BE THE "HOTTEST" AREAS OF NUTRITION RESEARCH IN 2020?

Global Food Security

Collectively, global food security, food safety, and sustainability warrant urgent action and will be among the most pressing topics in nutrition research in 2020. Global concerns regarding ways to safely feed more than 8 billion people on Earth in 2020 in the face of global climate change will likely overshadow the microcosm of issues on a local or national level [1]. Sufficient food may be available to feed everyone on Earth in 2020, but economic and political issues will likely hinder appropriate distribution [2]. Water is an essential nutrient, and access to clean water is also among the most pressing global health challenges.

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The development of genetically modified (GM) food crops to increase nutritional content will receive increased scrutiny and controversy. Increased beta-carotene content in rice (golden rice) and bananas has already been achieved through genetic modification, and these 2 staple crops have the potential to save the lives and eyesight of millions of children in a simple, cost-effective manner. Though the current evidence indicates that these GM crops are safe and effective, controversial perspectives regarding unknown environmental damage limit the scaling up of these crops to large commercial production. The debate over GM rice and bananas, as well as other crops, will likely continue and indeed intensify well into 2020.

Juxtaposed to the issues of food security is the rising incidence of obesity and diabetes on a global scale in both developed and developing economies [3].

Solutions to global food issues will ultimately be dependent on harmonization and partnerships among government, non-governmental organizations, industrial corporations, and individuals.

Microbiome/Microflora

An estimated 100 trillion microorganisms reside in the body, which is more than 10 times the number of human cells. By 2020, a more clear understanding will exist about dysbiosis, the disruption of homeostatic balance between the microbiota and the host, which has already been implicated as a factor in the development of numerous diseases, including obesity and type 2 diabetes. Disease prevention, treatment, and even cure may center on regulating the type and amount of microbiota in different regions of the body. It is important to more clearly define which microbiome is being considered, because different microbiota populations exist in the gut, the skin, the vaginal tract, the upper respiratory tract, and other body locations. Studies that explore effects of nutrition, dietary supplements, and physical activity need to focus on specific microflora populations or the interrelationships among populations. By 2020, a better understanding should exist about how changes in the gut microbiome may affect microbial populations in other parts of the body [4].

Improved "-omic" technologies and computing power will enable researchers to assess the influence of diet and the environment on various microflora populations, including an understanding of the diversity and relative size of different microbiotic members [5]. High-throughput analysis now makes it possible to rapidly assess the effects of foods, beverages, and supplements on select microbiomes. Future efforts will also focus on how changes in metabolic activity of these microbiomes may affect human health.

The microbiome established during early development may influence the risk for diseases later in life. Recent data support the concept that, even in the case of very similar genetic backgrounds (twins), seemingly small differences in the gut microflora can have a significant influence on the risk of developing obesity. A greater understanding of these dynamics will support individualized programs to help with weight management. It is a reasonable prediction that by 2020 the role of the gut microbiota will be appreciated for its influence in obesity [6], immune regulation, and the risk of several diseases, including cancer, gastrointestinal disorders, neurodegenerative diseases, and, possibly, the aging process.

The role of secondary metabolites from bacterial processing of components in fruits and vegetables and the genetic and epigenetic variability involved will be better understood by 2020 [7]. For example, both green tea and pomegranate ellagitannins are metabolized by microflora to secondary metabolites, including phenolic acids and urolithins, respectively, in animal models [8]. These and possibly other flavonoids have effects on bacterial growth *in vitro*, and future research is needed to explore and extend these exciting observations to humans. An improved understanding of the effects of diverse phytochemicals on the profile of microflora in different microbiomes will likely lead to changes in agricultural practices and food processing techniques that amplify the amount and availability of health-promoting phytochemicals.

Gene Expression

Another major topic in 2020 will be the nutritional programming of gene expression, both in the human genome and in our associated microflora microbiome [9]. The role of macro- and micronutrients and well-defined phytochemicals in regulating genetic expression will be well accepted, and transgenerational effects will also be clarified [10]. Strong evidence already exists that short stature, based on intrauterine programming, increases the risk of obesity and that changes in the associated epigenetics can be passed from one generation to another. One of the biggest questions by 2020 will be how many other diseases have their roots *in utero* and in early development and how nutrition might change possible negatives trajectories.

All humans are approximately 99% genetically identical, but the remaining 1% differences can have a marked influence among normal individuals with respect to how they utilize foods, their susceptibility to nutritional deficiencies and toxicities, their response to xenobiotics, and their risk for many food allergies. Advances in our understanding of the interaction of specific phytochemicals and gene expression will also lead to a better understanding of the potential health benefits of individual plant foods. For example, 50% of normal individuals have a mutation in glutathione S-transferase M2, which renders the enzyme nonfunctional. This enzyme helps the body eliminate isothiocyanate, a toxic chemical resulting from the metabolism of glucoraphanin found in broccoli and other cruciferous vegetables. Regardless of whether this mutation is present, eating more than 3 servings per week of broccoli is associated with a reduction in the incidence of colon polyps of approximately 20%. However, individuals with the null mutation have an

observed 50% reduction in polyps. The null mutation is associated with increased blood levels of isothiocyanate after eating cruciferous vegetables, which in turn leads to the induction of other glutathione-S-transferase enzymes in the same family [11].

Expanding understanding of the extent to which nutrition can affect gene expression will lead to an increasing awareness that dietary advice should take into account an individual's genetic background. By 2020, personalized diet and nutrition recommendations will become increasingly common. The implications of this for sales of nutritional supplements and nutraceuticals foods and beverages will be vast. While large segments of the U.S. population do not achieve the suggested intake of some vitamins and minerals through food alone, solutions may revolve around individualized needs based on genetic and epigenetic profiles, rather than the current suggestions based on age- and sex-specific recommendations [12]. Additional implications are likely for meal planning at public institutions (e.g., schools, military settings, prisons) and in public health planning for low-income populations.

Energy Metabolism

Data from the U.S. Centers for Disease Control and Prevention, the American Heart Association, and other authoritative bodies clearly indicate that obesity will continue to be the top nutrition- and health-related priority in 2020. The global economic cost of obesity, and the treatment of its comorbidities, including diabetes and vascular disease, will continue to escalate. Though the causes of obesity are multifactorial in nature, the overall result is from an imbalance between energy intake and energy expenditure.

Viewing energy balance as a multidimensional system, rather than as isolated parts that somehow work together, will likely be one of the hottest topics in 2020. A better understanding of energy balance and energy flux will likely provide new insights and solutions to address the obesity problem, in both developed and developing countries. Energy balance is more than just "calories in and calories out" because factors such as energy utilization and energy storage must also be considered [13,14]. Improving the accuracy of measurements for assessing dietary intake and energy balance is needed, because these tools are needed to guide public policy, to help industry formulate healthy new products, and to drive the research agenda [15].

One strategic use of nutrition to enhance bioenergetics will be a focus on cellular energy and mitochondrial function. Mitochondrial dysfunction has been linked to severe acute illnesses such as sepsis, to chronic degenerative disease states involving all the major organs and may be centrally involved in the aging process. Dietary manipulations and use of certain food components or supplements may be a means to enhance mitochondrial function and thus affect energy metabolism and energy fluxes in the body. Strategies will be developed to consider genetic and epigenetic factors in bioenergetic manipulations, with further individualization based on factors such as sex and age. The role of the intestinal microbiome in maintaining cellular energy homeostasis will be better understood, and it will increasingly become a target for manipulation [16,17].

By 2020, it can be estimated that close to 2 million people in the United States and Canada alone will have had gastric bypass and other forms of bariatric surgery. Given that a growing number of adolescents are obese, the population of bypass patients will increasingly include young individuals who are obese or morbidly obese. Is it appropriate that daily recommended intakes of vitamins, minerals, and other essential nutrients developed for normal-weight people be applied to these groups? Gastric bypass establishes a pattern of impaired micronutrient absorption. Morbid obesity impairs vascular endothelial function and glucose regulation and increases systemic inflammation. It is important to define nutritional strategies and dietary supplements that can help mitigate these dysfunctions.

Addressing the obesity epidemic requires a multifaceted approach and shared responsibilities between individuals, social networks, and governments at the national, regional, and local levels and responsible innovations and marketing by members of industry, including food, beverage, and dietary supplement companies [18,19].

Many popular diet suggestions lack scientific evidence of efficacy yet appeal to consumers' emotions in an attempt to find quick and easy solutions to the obesity problem. Proposals to place taxes and restrictions on high-calorie or high-sugar foods and beverages continue to be advanced, with minimal evidence that such actions are effective and no clear consensus of what "high-calorie," "high-fat," "high-sugar," or "bad" foods or beverages means [20]. Unlike tobacco smoking, where overwhelming evidence exists regarding negative health impacts and where taxation has reduced consumption, a similar approach for some foods and beverages is fraught with peril. Menu labeling may seem to be a reasonable approach to help consumers make wise food choices, but data showing that such labeling will alter people's behaviors is currently lacking. Innovative public health approaches are needed by 2020, but misguided approaches can do more harm than good, no matter how good the intention.

An estimated reduction of less than 10% in daily caloric intake or increases in energy expenditure would help achieve the U.S. federal government's *Healthy People 2020* goals for obesity. Multiple sustained and simultaneous community-based interventions are needed, and no single public health intervention is likely to be effective in reaching this target [21]. Relatively modest and achievable changes in the food supply have great potential to achieve meaningful benefits. New foods and beverages with reduced energy density and reduced portion sizes, along with innovations in packaging, are simple examples of what can be implemented by 2020 [22]. Advances in nutrition education and marketing that bring new health and nutrition messages to consumers will also help address the obesity epidemic [23,24].

Cancer

Nutritional therapies for cancer treatment are among the most difficult to study. Some cancers (e.g., pancreatic) develop quickly and therefore demand urgent medical treatment that typically excludes these patients from clinical nutrition studies. Other cancers evolve so slowly (e.g., prostate cancer under active surveillance) that relevant outcomes often require large numbers of subjects and years of follow-up. By 2020, genomic and metabolomic profiles and large dataset analysis will offer new opportunities to identify relevant indices and biomarkers and conduct timely, cost-efficient clinical interventions on nutrition and cancer.

Medical professionals will expand their thinking about the role of natural products to consider how they might complement conventional care, such as in increasing the effectiveness of chemotherapy or radiation. Though these therapies often improve the outcome of cancer treatment, patients sometimes are forced to discontinue such treatments due to severe adverse effects that reduce their quality of life. Reductions in dosing and/or duration of medical treatment can render the therapy less effective than intended, and it is vital that safe new approaches to reduce side effects be discovered. Two such therapies currently being tested at Osaka University School of Medicine are the use of Active Hexose Correlated Compound, a shiitake mushroom mycelium extract, among advanced cancer patients receiving chemotherapy and the role of L-glutamine supplementation in reducing the severity of mucositis among patients with cancer in the oral cavity [25,26].

Inflammation

Nutritional strategies to reduce inflammation will address many of the underlying issues related to chronic diseases such as vascular disease and certain forms of arthritis. Future nutrition research will likely focus on the role of diet and nutraceuticals to help moderate inflammation and possibly reduce the risk of cancer [27]. It is incumbent on nutrition scientists to identify foods, beverages, and dietary patterns that are both pro-inflammatory and anti-inflammatory. A balance of inflammation is important, because too much can lead to acute or chronic disease, and too little may impair wound healing or increase susceptibility to infection. By 2020, one may possibly put a small device or test strip in one's mouth to give a real-time readout on one's inflammation status. Such information can be used by consumers, working with health care professionals, to help them make food and supplement choices to keep their inflammation status in an ideal balance.

Aging

An important nutrition topic in 2020 will be the needs of an aging population. In Japan, 25% of citizens are over the age of 65 years, making it the world's first "super-aged society" [28]. Though the average life span of a Japanese woman is 86.5 years (ranking first in the world) and that of a Japanese man is 79.9 years (ranking fifth worldwide), the most important issue is healthy life expectancy, not the average life span. Who wants to live a long and unhealthy life, where quality of life deteriorates slowly and for a long time?

In addition to chronic diseases such as cancer and vascular disorders, nutrition research must focus on other serious problems among older people, including obesity [29], metabolic syndrome, locomotive syndrome, cognitive impairment [30], and problems related to taste, mastication, and swallowing. Recent discoveries of systemic factors from young animals that induce vascular remodeling and enhance neurogenesis in mice may be extended to humans by 2020 [31]. The potential identification of foods and food components that stimulate the production of factors that accelerate tissue repair and regeneration could revolutionize dietary recommendations across multiple age groups and be further individualized based on genetic and epigenetic profiles.

Bioengineering

If genetics play as important a role in one's nutritional requirements as is currently thought, methods will likely be in place that allow assessment at an individual level, rather than at a population level, and that determine the value of realistic and subtle dietary changes.

The development and use of new monitoring technologies and tools that individuals might use to better follow their nutritional and health status will be one of the hottest topics in 2020. Advances in bioengineering will continue to bring new approaches to clinical nutrition and to nutrition education. We live in a time where individuals expect rapid responses to their actions, whether it is the text message they just sent or to changes in their diet. Increasingly, consumers will expect that if they adopt "positive" changes in their diets, then clear evidence of their actions will follow quickly. Given the rising costs in health care and the overwhelming evidence that prevention is less expensive than treatment of disease, rapid and individualized feedback on an individual level will be an excellent way to motivate people to make adjustments in their diet and maintain a course of health promotion. In the past, pedometers worn on the belt gave feedback regarding physical activity (e.g., the common goal of walking 10,000 steps each day), whereas today, smart phones and bands worn on one's wrist can provide immediate feedback on activity, pulse, and a myriad of other health-related outcomes. By 2020, smart technologies that use noninvasive assessments, such as breath, saliva, urine, and stool sampling (smart toilets linked to refrigerators and mobile devices?), coupled with relevant biomarkers and individualized to a person's genetic and epigenetic profile, will be able to provide real-time data to help motivate people to make appropriate food and lifestyle choices.

Nutrition Education

More sophisticated methods to motivate people to make healthy food choices are needed. Providing nutrition knowledge alone rarely results in sustained behavior change, and even diagnosis of a disease does not always lead a person to make lasting dietary and lifestyle changes. Food choices are very personal, and modification of food intake is a complex issue that requires much new research. Although educators can provide people with multiple types of useful information, food choices usually are based on 4 factors: flavor, economics, availability, and convenience.

Further development of "high touch-high tech" solutions will occur by 2020. For example, in Los Angeles County, the incidence of obesity varies widely by region, and factors such as social support, access to fresh fruits and vegetables, food insecurity, and access to health care all impact this incidence. A better understanding of social networks is needed so that public health programs can be implemented to take advantage of the psychologically contagious dynamics of weight management in a positive manner.

Dissemination of nutrition messages will be common on social media platforms. Research is needed to identify which messages and vehicles will effectively reach which audiences to effect behavior change. Social media will continue to bring health experts directly into contact with consumers. However, no regulatory filter exists on social media channels, and much misinformation about nutrition is currently circulated. Information overload is another issue that requires increased consideration, because many consumers simply ignore important and accurate nutrition advice when it is mixed with a barrage of unsubstantiated claims or when nutrition recommendations appear to be continuously changing. Taking responsibility for nutrition and health content in social media, while preserving freedom of expression, will be among the biggest challenges in this area by 2020.

Interdisciplinary and Cross-discipline Collaborations

A multidisciplinary approach to nutrition research will be firmly established by 2020, and teams of researchers will work together on most studies. Emphasis on translational research will be more common, requiring collaborations among those in basic and clinical research, nutritional epidemiology and biostatistics, food science, nutrition communications, public policy, and scientific ethics. Teams of researchers rather than individual scientists will produce answers to the most critical health issues, working across disciplines to bring a holistic and more representative approach to successful and sustainable solutions. Funding sources will be convinced that the era of independent science by a sole principal investigator is over. More large-scale, consortium-based research projects will be funded in areas such as the microbiome. Achievement and career advancement will continue to value scholarship and innovative ideas but will increasingly reward teamwork.

With limited resources and the increasing cost of biomedical research, diverse collaborations between academia, industry, and governments will be common. Pilot funding for innovative ideas, with only a select few showing the greatest promise being considered for further funding, may be a method to best target resources. This model, already employed by organizations such as the U.S. Agency for International Development and the Bill and Melinda Gates Foundation, will become increasingly common. Application of this model to nutrition research by 2020 will encourage scientists to develop numerous areas of expertise, rather than focus on a single nutrient to define one's career.

The importance of nutrition in treating and preventing acute and chronic illness will be increasingly emphasized by health professionals (physicians, nurse practitioners, physician assistants, pharmacists, physical and occupational therapists, etc.). Cross-training and licensure or certification in nutritional sciences will be more common, because consumers and patients will demand evidence of authority and knowledge about nutrition, rather than just believing the latest marketing hype or some unsubstantiated story perpetuated on the Internet [32].

Future career paths will likely not look like they do presently. Employers are already searching for and, in some cases, training individuals in more than one career skill with depth in multiple areas. Business acumen, including project and personnel management skills, will be very beneficial to help members of academia in their grant writing and to partner with those in industry to understand their needs and timelines. Business management is also essential for development of cross-functional public–private programs and partnerships and for fostering small business ventures, which are at the core of most economic growth and breakthrough innovation. A desire for work–life balance or, more likely, work–life integration, an emphasis on quality of life, and having fun with passion for one's work, will be more valued by 2020 than currently.

SUMMARY

Advances in nutrition research by 2020 will help people live healthier, longer, and more productive lives. Personalized nutrition and medical strategies will be common, based on a greater understanding of microbiomes and gene expression. New approaches will help address diseases such as obesity and cancer and underlying causes of inflammation and aging. Innovative devices will help guide people toward their lifestyle goals, and novel public health and nutrition education programs will empower people to make wise food and lifestyle choices. Combined efforts will be common, as teams of researchers pool their skills to address the most pressing health issues on global and individual levels. Greater collaboration among members of academia,

industry, and government will be needed to address both global and local nutrition and health issues.

The strong consensus of the panel was that advances in nutrition research by 2020 will address the most urgent health issues on a global and individual level. Personalized nutrition and health care strategies will be common, based on a greater understanding of the importance of one's genetic background, as well as how their diet may influence their microbiome. New approaches will help address the causes as well as the treatment of a number of diseases including obesity, cancer, and numerous age-associated diseases. An improved understanding of how diet can help regulate inflammation and the immune system will provide insights for health promotion and disease prevention and treatment. Innovative devices will support people toward their lifestyle goals, and novel public health and nutrition education programs will empower people to make educated food and lifestyle choices if they chose to do so. In contrast to investigators primarily working on their own, large, integrated research groups that reach across multiple disciplines will be more common. Greater collaboration is likely among members of academia, industry, government, and nongovernmental organizations, with the goal of providing innovative and cost-effective solutions to help people enjoy healthier, longer, and more productive lives.

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